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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/018,194	02/04/1998	BARBARA A. GILCHRIST	BU94-15A2	9447

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EXAMINER	
WEGERT, SANDRA L	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 01/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/018,194	GILCHREST ET AL.	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/29/04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33-36 and 45-55* is/are pending in the application.

4a) Of the above claim(s) *45-52,54 and 55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-36 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 May 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of Application, Amendments, and/or Claims

Applicant's election of Invention I, (Claims 33-36 and 53) in the Paper submitted 29 September 2003, is acknowledged. Applicant had previously elected the following Species: SEQ ID NO: 9. It should be noted that claims will be examined insofar as they read on the elected Invention. Claims 45-52 and 54-55 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Applicant elected Invention I with traverse. The traversal is on the ground(s) that similar claims in the previous Restriction requirement were joined together in the same inventive group. Applicant's arguments are not persuasive, however, since Claims 33-36 and 37-44 have been amended subsequently and thus recite new inventions or clarify existing claimed inventions. For example language in the original Claim 33 was somewhat ambiguous as far as "maintaining" hair growth and "inducing" hair growth, whereas newly-presented Claim 33 reads only on "maintaining" hair growth. Inventive Groups I and II in question were properly restricted as the methods are practiced with materially different process steps for materially different purposes and each method requires a non-coextensive search because of different starting materials, process steps, goals and measured endpoints. As explained in the last Restriction Office Action (8/21/03), the method of group II requires human patients with Alopecia Areata, while the method of group I does not. Therefore, the search of the art for the method practiced with the disease of group II is different from the search for the methods of Invention I. As well, enablement issues are very different when discussing treatment of humans

that have a poorly-understood disease versus preventing apoptosis of cells in a vertebrate or in tissue culture. In addition, since a complete search of the art includes a search of the art that renders an invention obvious as well as anticipatory, the additional searches required for examination of Invention I *with* Invention II would be extensive, thus presenting an undue burden for the examiner.

The requirement is still deemed proper and is therefore made FINAL.

Claims 33-36 and 53 are under examination in the Instant Application.

Claim 53 is objected to because it recites or encompasses non-elected inventions.

Appropriate correction is required.

35 USC § 112, first paragraph - lack of enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 33-36 and 53 are rejected under 35 U.S.C. 112, first paragraph, because the subject matter was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification is not enabling for the limitations of the claims wherein hair growth in a vertebrate is maintained by contacting keratinocytes with a ligand of receptor p75.

Claims 33-36 and 53 read on a method of maintaining hair growth in a vertebrate by contacting keratinocytes with peptides comprising KGA (lysine-glycine-alanine), such as SEQ ID NO: 4 and 9, with the requirement that peptides used for the claimed methods are biologically active fragments of nerve growth factor.

The specification discloses the use of ultraviolet light to cause apoptosis of cultured keratinocytes and describes experiments in which NGF enhances cultured keratinocyte survival after UV irradiation. The specification also describes correlations between bcl-2 levels and NGF concentrations bathing the cells, thus implying an apoptotic mechanism for keratinocyte cell death caused by UV irradiation-because, for example, this tumor-suppressor gene has been found to be important in apoptotic mechanisms that prevent proliferation of cancerous cells. Several ligands are disclosed in the instant Specification: the cyclic decapeptide CATDIKGAEC- SEQ ID NO: 9-, the fragment CKGAIC and the "KGA" fragment of SEQ ID NO: 9. Both the CATDIKGAEC and the KGA peptides are high affinity ligands for p75, binding at nanomole/liter concentrations (Yaar, 1995, J. Invest. Dermatol. **108**:568a).

However, the claims read on a method of maintaining hair growth in a vertebrate by inhibiting apoptosis in keratinocytes by adding the peptide CATDIKGAEC (SEQ ID NO: 9), for example, or fragments of SEQ ID NO: 9 comprising the KGA peptide. There is no enabling discussion or working examples disclosed in the instant application as to how to practice the method of maintaining hair growth (presumably for a time beyond what occurs naturally) in the epidermis of a vertebrate. Maintenance of hair growth on a patch of skin is subject to different conditions based on many factors. These factors may include: the type of hair follicle; the

location of the patch of skin (for example, the scalp may have different properties than other areas); reproductive steroid levels; anticancer drugs or radiation, as well as possible autoimmune factors. Many factors interact, or are poorly understood (Ben-Ari, 2000, Bioscience, **50**: 303-308). It seems clear that apoptosis of *cultured* keratinocytes caused by irradiation with UV light is a poor model of hair loss in a mammal. This is because the follicle is made up of several cell types in addition to keratinocytes. Also, not all (or even most) keratinocytes grow hair. In addition, although hair follicles have been shown to be killed or pushed to the telogen stage by radiation (for example in cancer patients), the effect is only temporary. Thus, radiation, either in cultured cells or in dermal follicles, does not cause a condition that mirrors the hormone-related *permanent* hair loss seen in male pattern baldness nor the immune-related long-lasting hair-loss seen in Alopecia areata, nor in any other condition for which hair is lost or there is a need to maintain hair loss.

Furthermore, the claims read on a method of maintaining hair growth in the vertebrate epidermis by inhibiting apoptosis in keratinocytes using "KGA" ligands and antibodies. However, the ligand disclosed in the specification as used for the method of the invention is Nerve Growth Factor or NGF. There is no reason to infer- because NGF inhibits apoptosis in the damaged cells- that the peptide of SEQ ID NO: 4 and 9 and *KGA* will do the same. The peptides of SEQ ID NO: 9 and *KGA* are small fragments of the large β-subunit of NGF, and have been shown to bind p75 (Yaar, M, et al, 1995, J. Invest. Dermatol. **108**: 568a). However, the mechanism of NGF's anti-apoptotic action may involve receptors other than p75, such as TRK-A receptors (Zigmond, (ed), 1999, Fig. 21.6).

Due to the large quantity of experimentation required to determine how to use the disclosed SEQ ID NO: 9 and *KGA* to induce hair growth in a vertebrate, the lack of direction or guidance in the specification regarding the same, the lack of working examples that apply SEQ ID NO: 9 and *KGA* to the skin of a vertebrate in which a condition has caused hair loss, the state of the art showing the complexities of hair loss syndromes, and the breadth of the claims which embrace many types of hair loss syndromes, --undue experimentation would be required of the skilled artisan to make and use the claimed invention in its full scope.

Conclusion

No claims are allowed.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (703) 308-9346. The

examiner can normally be reached Monday - Friday from 8:30 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SLW
1/24/04

Gary L Kunz

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